10/820,537

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sudhir V. Shah		
Application No.:	10/820,537	Group:	1654
Filed:	April 8, 2004	Examiner:	Winston, Randall O.
Confirmation No.:	8841		
For:	DIAGNOSIS AND TREATMENT OF HUMAN KIDNEY DISEASES		

CERTIFICATE OF MAILING OR TRANSMISSION

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DECLARATION OF SUDHIR V. SHAH, M. D., UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Sudhir V. Shah, M.D., of 2 Isbell Lane, Little Rock, Arkansas 72223, declare as follows:

A. I received my Doctorate of Medicine degree from Grant Medical College in Bombay, India in 1971. I received my Board Certification in Internal Medicine in 1975 and an additional Board Certification in Nephrology in 1982.

B. Currently, I am Head of the Division of Nephrology at the University of Arkansas for Medical Sciences in Little Rock, Arkansas and President of Shiva Biomedical, LLC (hereinafter "Shiva"). Shiva is the Assignee of the entire right, title and interest in U.S. Patent Application No. 10/820,537.

C. My responsibilities at Shiva include direction of scientific programs, including human clinical trials, specifically with regard to initiating and designing investigations into methods of treating humans with kidney diseases, in particular, human clinical studies involving the treatment of humans with kidney diseases by administering iron chelators.

D. I have read U.S. Patent Application No. 10/820,537 and the Office Action mailed from the U.S. Patent and Trademark Office on September 10, 2004. I understand the application, the pending Office Action and the issues related to patentability presented by the Examiner in the Office Action for the invention claimed in the patent application.

E. In support of the reply to the Office Action, I hereby state the following:

1. Shiva has conducted additional experiments, since filing of U.S. Application No. 10/820,537, which show that the administration of an iron chelator to a human having microalbuminuria is efficacious in improving renal function, as shown in the accompanying Tables attached to this Declaration as Appendix I. The additional human studies were conducted employing techniques and doses of iron chelators as described in the U.S. Patent Application No. 10/820,537. A brief description of the experimental procedure follows.

2. Thirty (30) diabetic patients with microalbuminuria (17 males and 13 females) with a mean age of 51 were orally administered deferiprone at a dose of 50 mg/kg per day for nine months. The iron chelator was

administered three time a day. Diabetes was confirmed by blood glucose measurements. Microalbuminuria was confirmed by an albumin radioimmunoassay (Immunotech, France). Catalytic iron in the urine of patients before, after and during treatment with deferiprone was determined employing the assay as described in U.S. Patent Application No. 10/820,537 with the exception that the assay was not standardized. Improvements in renal function were assessed by measuring urinary protein (milligram of albumin per milligram of creatinine) before, during and after deferiprone administration throughout the nine month treatment period. Indices of adverse side effects (i.e., white blood cell counts, total bilirubin, hemoglobin) were also assessed throughout the treatment period.

3. As shown in Appendix I, subjects treated with deferiprone have a decrease in the urinary protein at six and nine months following treatment. A decrease in urinary protein is a well-recognized indices of improved kidney function.

4. The standard curve employed to extrapolate the amount of catalytic iron in the urine was a standard curve generated based on prior assays and not run in parallel with each assay. Thus, the assay employed to measure catalytic iron in these studies was not standardized. Despite the lack of standardization of the assay, a trend in a decrease in catalytic iron in the urine of subjects treated with the iron chelator occurred during the treatment period.

5. Minimal side effects were observed following the administration of the iron chelator for nine months. Thus, use of the iron chelator does not appear to adversely affect the health of the subjects.

6. It is my opinion that, these additional data, which are supported by the application as filed, show that administration of an iron chelator can treat

microalbuminuria in a human.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements, if made, may jeopardize the validity of the application or any patent issuing thereon.

Sudhir V. Shah

Sudhir V. Shah, M.D.

12th January, 2005.

Date

APPENDIX I

	Initial	n	9M	n
Weight kg	65.11±2.03	28	66.33±1.96	30
Hemoglobin g/dL	12.78±0.01	28	11.75±0.12	28
WBC 10^3/mL	7282±170	28	7077±172	30
PMNs %	70±1	28	73±1	30
Platelets x10^3/mL	2.76± 0.09	28	2.87±0.08	30
SGPT U/L	20±1	28	22±1	30
SGOT U/L	20±1	28	23±1	30
Total bilirubin mg/dL	0.90±0.00	28	0.95±0.03	30
Alk.PO_4 U/L	99±1	28	103±1	30
HbA1C (%)	7.31±0.21	30	8.11±0.35	30
Serum iron µg/dL	111±17	30	73±5	30

microalbuminuria mg albumin/gm creatinine (normal <30; microalbuminuria 30-300)			
	Mean	n	P
Initial	96±14	30	
6 Months	42±15	30	0.003*
9 Months	27±8	28	<0.0001**
µg albumin/min (normal <20 microalbuminuria 20-200)			
	Mean	n	P
Initial	78±13	30	
6 Months	42±16	30	0.02*
9 Months	22±7	28	<0.0001**